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Review article

Do women aged over 40 need different counseling on combined hormonal contraception?

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ABSTRACT

There is still a risk of pregnancy during the menopause transition, for most women after the age of 40, as occasional, spontaneous ovulation can occur. Women in this age group may therefore consider using contraception and want appropriate counseling. Aging is accompanied by changes that can increase the risks associated with the use of combined hormonal contraceptives (CHCs), but we do not have sufficient evidence to determine whether age alone increases the risks of using CHCs or whether there are additional risks if CHC use begins at an earlier age. Another issue is whether we can differentiate between initiator versus continuation influences on risk. The objective of this article is to review the risks associated with CHC to determine whether there is a need for more appropriate contraceptive counseling for women aged over 40.

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1. Introduction

A priori reasons forced us to conclude that contraceptive counseling needs to be diversified and age appropriate. Women over 40 have lower rates of contraceptive failure with any method than younger women because their fertility is lower, their sexual activity is less frequent, and they show greater compliance with contraceptive use. However, age increases the risk for some diseases and therefore requires a new risk-benefit balance regarding the use of contraceptive methods [1].

These elucidations are especially applicable to combined hormonal contraceptives (CHCs). The standard contraceptive history should focus on their medical history, since women with stroke, cardiovascular disease, migraine with aura and smokers should avoid CHCs. Other important medical history includes previous venous thrombosis (VT), malignancy and the medication history. Women over 40 years who request CHC require checking of blood pressure at the beginning and at least every six months [2].

In contraceptive counseling it is also essential to explain their non-contraceptive benefits, highlighting specific benefits for this group age, and put into context the risks –better in absolute terms- for each individual woman. In a previous article, we describe the *new* non-contraceptive benefits, as well as the *classics* in the cyclical instability, symptoms of menopause, bone density and vaginal dryness for methods containing estrogen in women over 40 [3]. The objective of this article is to review the risks associated with CHC to determine whether there is a need for more appropriate contraceptive counseling for women over 40.

2. Risks of CHC in women over 40

2.1. Age as a risk factor

The 'pyramid-shaped' structure of Europe's population indicates that the middle-aged individuals currently represent the largest age group. However, the use of CHCs is generally seen as acceptable for young people because clinical trials were mostly carried out on this age group and a fear exists that side effects may occur in other age groups.

Age represents the most important risk factor for conditions such as thrombosis, stroke or cancer. Therefore, we are in a complex dilemma: age is accompanied by changes that can increase the risks associated with CHC use, but we do not yet have enough evidence to fully determine whether age alone increases the risk of using CHC. In this direction, most of the evidence regarding the risks of CHCs is derived from studies of oral CHC use in women younger than 35 years of age, results from which have been extended to older women [4]. In addition, although there appears to be consensus that age alone does not imply any limitation in the use of CHC [5], however age is associated with an increased risk of venous thrombosis, which increases after age 39 among women using CHC pills [6].

We must not forget that pregnancy itself raises the risk of VT three-fold compared with the use of CHC and that pregnancy-related mortality among women over 40 is five times that of women under 30 [7].

2.2. Initiation versus continuation

Contraceptive counseling for women over 40 with medical conditions can be complex and requires an individualized approach. The question is whether we can differentiate between initiator versus continuation influences on risk. Certainly, some risks differ if CHC use begins in middle age or if use is continued from young ages. Thus, the thrombotic risk increases with age and is greatest in the first months of use [8]. Additionally, the presence of other cardiovascular risk factors (e.g., obesity, smoking, hypertension, and diabetes) highlights the importance of eligibility criteria and may even contraindicate the use of CHC with ethinyl-estradiol (EE) [9]. Furthermore, the risk of cervical cancer increases after continuous use for more than five years in women with human papillomavirus, and breast cancer data are conflicting and do not demonstrate a clear risk at any age in either of these two conditions [10,11].

2.2.1. Thrombosis

Age is associated with an increased risk of venous thrombosis (VT), which increases after age 39 among women using oral CHC. Estrogen increases the risk of VT, even when matched for other risk factors (RF), including obesity, smoking, diabetes, hypertension or thrombophilia. Therefore, CHC use should be avoided or undertaken with extreme caution in women over 40 who have any of these RFs [12].

In women over the age of 40, the risk of VT is twice that of women aged 20–24. This risk increases with estrogen dose and appears at the beginning of use, likely due to early exposure to thrombophilia [13]. Therefore, we consider this to be a potential risk for women over 40 who initiate the use of CHCs. As in the case of younger women, there is no reason to test for congenital thrombophilia if there is no family or personal history of thrombosis.

However, the latest revision of the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) did not issue a cause for concern or new reasons that alter the balance between the risks and benefits of CHC. This report established different risks depending on the progestogen and mentioned age as an isolated factor of thrombotic risk. However, these risks are independent of age, and at no point in the document did it state that the use of CHC must be restricted in women over 40 [14].

2.2.2. Myocardial infarction

Epidemiological studies have reported an increase in myocardial infarctions (MI), which are believed to be associated with a thrombotic mechanism rather than with the development of atherosclerotic plaques and an increase in cardiovascular mortality in CHC users who smoke and are over 35 [15].

Another large, prospective study from Sweden that included 1761 current CHC users between 40 and 49 years of age found no increased risk of MI among former or current CHC users. It also found that the initiation of CHC use in women 30 years of age or older carried no higher risk of MI than did initiation at age 29 or younger [16].

A meta-analysis shows that the use of CHCs containing high-dose estrogen is associated with an increased MI risk (OR 2.5, 95% CI 1.9–3.2), although this has not been observed in the past among users of CHCs with low-dose estrogen [15].

A consensus panel suggested that CHCs should not be given to women over 35 who smoke more than 15 cigarettes per day, but they can be considered in women who smoke fewer than 15 cigarettes per day, even for those >35years old who have an occasional cigarette, since the risks of pregnancy in this age group are greater than the risks associated with OC use [17]. However, we agree with those who consider that smoking above the age of 35 is a contraindication to the use of CHC [18]. The relationship between smoking, the use of oral CHC and CVD may be associated with high concentrations of intravascular plasma fibrinogen and fibrin deposition and with the enhanced expression of tissue factor from monocytes. In addition, CHC should be avoided in women over 40 with obesity, hypertension or migraine headaches, in which case could be candidates for progestin-only contraception [19]. On the other hand, cardiovascular events are rare among e-cigarette users in the general population and that e-cigarettes may affect heart rate and blood pressure less than conventional cigarettes [20]. Anyway,